HYPERCALCEMIA IN 32 Y OLD MAN WITH SARCOIDOSIS AND PARAPLEGIA

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Abstract

Introduction: Hypercalcemia of immobilization is rare, but hypercalciuria is more common than hypercalcemia. Hypercalcemia an uncommon presentation of sarcoidosis occurs in 5 to 10% of patients, but 30 to 50% has hypercalciuria. The cause of hypercalcemia in sarcoidosis is similar to other granulomatous diseases, and increased activity of 1 alpha hydroxylase.

Case report: A 32-year-old man with a history of car accident and severe trauma to lumbar spine. High serum calcium was reported (14.6 mg/dL) in his laboratory data. Chest computed tomography (CT) scan revealed numerous nodules in parenchyma of both lungs. Chronic non-caseating granulomatous inflammation (more probably sarcoidosis) was reported. Prednisolone was started at a dose of 35 mg/day and 10 days after treatment serum calcium level decreased to normal range.

Conclusion: Hypercalcemia has been described in patients with granulomatous disorders, most commonly sarcoidosis. Treatment of the hypercalcemia or hypercalciuria in granulomatous disorders is aimed at treatment of the underlying disorder. Moderate-dose glucocorticoid therapy is typically used to treat sarcoidosis. The serum calcium concentration begins to fall in two days, but the full hypocalcemic response may take 7 to 10 days depending upon the prednisone dose.

Keywords: Hypercalcemia, immobilization, sarcoidosis

Introduction

Hypercalcemia has been described in patients with immobilization and sarcoidosis, although both diseases are uncommon (1, 2).

Hypercalcemia of immobilization is rare, but hypercalciuria is more common than hypercalcemia, this disorder is associated with increased bone resorption due to increased osteoclast activity (1, 2). The duration of inactivity has been reported from 10 days to several months, but the average is 4 months (3). However extensive evaluation is recommended to rule out other causes of hypercalcemia (4). Sarcoidosis is a chronic multi systemic granulomatous disease with unknown etiology, which affects multiple body organs such as lungs, eyes, skin and lymph nodes. But lungs are the most common involved organ (5).

Hypercalcemia an uncommon presentation of sarcoidosis occurs in 5 to 10% of patients, but 30 to 50% have hypercalciuria (6). The cause of hypercalcemia in sarcoidosis is similar to other granulomatous diseases, and increased activity of 1 alpha hydroxylase in macrophages leads to an increase of 1-25 hydroxyvitamin D (7) which increases the intestinal calcium absorption. Although osteoclast activity and bone resorption plays a role in sarcoidosis induced hypercalcemia. In this study we report a case of hypercalcemia associated with sarcoidosis and immobilization.

Case report

A 32-year-old man with a history of car accident and severe trauma to lumbar spine 4 months ago, which lead to spinal cord injury and paraplegia. Subsequently, the T12 (thoracic), L1 (lumbar) fixation was done for the patient. The patient was completely bedridden at home. One month later, he complained of nausea and vomiting, which gradually became more intense so he was investigated. High serum calcium was reported (14.6 mg/dL) in his laboratory data. Then he was admitted to endocrine ward for more evaluation. The patient stated a history of cough and shortness of breath in few years ago, which was improved with several injections of corticosteroid, but no further evaluation was done. He denied taking any Vitamin or other supplements. There was no family history of autoimmune disease and no history of smoking or alcohol consumption. On physical examination blood pressure =110/75 mmhg, body temperature = 37 Co ,

pulse rate = 80/min, body weight = 68 kg. He was conscious and oriented. And except decreased lower limbs force which was 1/5, other findings were unremarkable. In chest x-ray image multiple ill-defined densities were seen scattered in lung parenchyma with bilateral hilar adenopathy and mild scoliosis of thoracic spines (Figure 1).

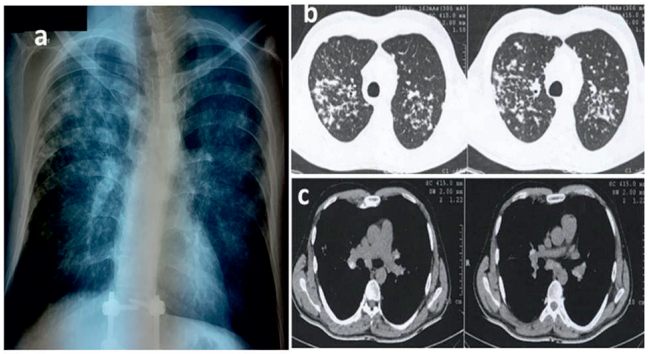

FIGURE 1. (a) chest x ray. (b) CT scan of chest (parenchyma view). (c) mediastinal view.

Chest CT scan revealed numerous nodules in parenchyma of both lungs (Figure 1) with mediastinal lymphadenopathies which calcification was noted in lymph nodes (Figure 1). The patient`s lab data are given in (Table 1).

TABLE 1. Lab data before and after therapy in patient

Parameters	At the time of accident	1 month after accident	2 month after accident	3 month after accident	After therapy
PTH pg/mL	3	5.6	-	4	-
Ca mg/dL	14.6	12.6	11.5	12	9.8
Ca Ion mmol/L	1.6	1.5	1.45	1.5	1.2
P mg/dL	3	4.1	3.5	3.8	4
25OHvitD ng/mL	41	56	-	48	-
Urine Ca mg/day	890	-	-	750	-
ACE U/L (normal 6±64)	-	48	-	67	-
Albumin g/dl	4				
ESR mm/h	30			25	
Hb g/dL	10.5		12		14
WBC x1000/Cumm	7.8				5.5
BUN mg/dL	45				20
Cr mg/dL	1.8				0.9
Na mEq/lit	148			139	
K mEq/lit	4			4	
FBS mg/dL	109		92		
TSH miu/lit	1				

Bone density was performed to further evaluation. In bone mineral density of patient Z score of 1/3 wrist, total hip and femoral neck were -3.2, -2.3 and -1 respectively and T score in these sites were -3.3, -2.4 and -1.2 respectively.

HIV and viral hepatitis serology were negative. Bronchoscopy for bronchoalveolar lavage (BAL) and Transbronchial lung biopsy (TBLB) was done. Tuberculosis was excluded. Interferon-γ release assay (IGRA) test and BAL for tuberculosis was negative in pathologic study of TBLB specimen and chronic non-caseating granulomatous inflammation (more probably sarcoidosis) was reported (Figure 2). Prednisolone was started at a dose of 35 mg/day and 10 days after treatment serum calcium level decreased to normal range (Table 1). The nausea and vomiting of the patient gradually improved. Muscle force was 2 out of 5 and daily physical therapies were performed for the patient.

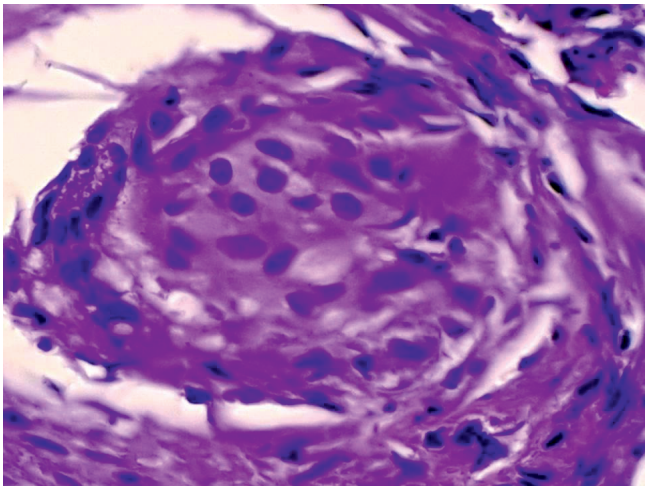

FIGURE 2. Histopathologic appearance of non-caseating granuloma of lung biopsy. (Hematoxylin – Eosin, original magnification ×100)

Discussion

Hypercalcemia is a common metabolic disorder which is mostly asymptomatic and often is detected accidently and divided into two categories, parathyroid hormone (PTH) dependent and PTH independent (8). The most common cause of PTH dependent hypercalcemia is primary hyperparathyroidism 8. PTH independent hypercalcemia can occur due to malignancy, granolomatos`s disease, Vit D toxicity, immobilization and hyperparathyroidism. Malignancy is the most common cause of hypercalemia in hospital (8). A diagnosis of granulomatous disease is important so we

should always think about it (9). In 1939 Harrell et al. for the first time mentioned sarcoidosis associated hypercalcemia. Immobilization from 10 days up to 1 year can cause hypercalcaemia and should be considered (3).

Sarcoidosis is an unidentified systemic granulomatous disease in which small nodules (granuloma) develop from inflammatory tissues in the organs of the body (10). Sarcoidosis often affects the lungs, but it can also affect the skin, eyes, heart, muscle, liver, spleen, intestine, kidneys, testicles, nerves, lymph nodes, joints, and brain (5). The exact cause of sarcoidosis is not known. A theory that the disease is genetically predisposed to people is contact with certain environmental factors. Although these specific factors are unknown, many organisms, including viruses and bacteria, have been identified as the potential cause of this disorder (10). Due to the lack of a single test for the diagnosis of sarcoidosis, the diagnosis of the disease is based on various factors such as clinical signs and symptoms, laboratory data, chest X-ray and microscopic study of tissue samples for rule out of other granolomatos diseases such as tuberculosis and lymphoma (8). A biopsy is usually recommended for non-caseating granuloma detection (8). Sarcoidosis causes Angiotensin Converting Enzyme (ACE) secretion in 60% of cases. But its level is not determinate of prognosis and it has a low sensitivity and specificity (9). Hypercalcemia in sarcoidosis is rare and the cause is the same as other granulomatous diseases. sarcoidosis associated hypercalcemia is due to increased activated form of vitamin D in the mononuclear cells (especially macrophages) of alveolus and lymph nodes (6). Our patient had a history of cough and shortness of breath in the past years, which was recovered with short time use of corticosteroid, but, unfortunately, the supplementary study was not performed and probably sarcoidosis was arisen since then. The possibility of bilateral lymph node calcification in the lung CT scan reveals the probable chronicity of disease. The bone density in the vertebrae was not performed because of the history of fracture and spine fixation. Bone density in the wrist area was much lower for the patient's age, sex and ethnicity (Z score = -3.2). Therefore, because of a significant decrease in bone density, we can conclude that hypercalcemia has been existed for many years and exacerbated by immobilization. Thereafter the patient was symptomatic and had nausea and vomiting, and hypercalcemia was detected.

Conclusion

We are reported a patient with immobilization and hypercalcemia. Hypercalcemia and low-PTH were observed in this study. After further studies, sarcoidosis was proven to the patient. This patient has had sarcoidosis and hypercalcemia over the past years (due to the presence of calcification in the hilar lymph nodes and reduced bone density) and hypercalcemia was intensified by paraplegia. The patient's hypercalcemia improved with corticosteroid therapy after 10 days.

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